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Intraoperative fluid irrigation for traumatic wounds (Protocol)

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[Intervention Protocol]

Intraoperative fluid irrigation for traumatic wounds

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effects of intraoperative fluid irrigation in preventing wound infection in traumatic wounds.

BACKGROUND

Description of the condition

Wounds caused by traumatic injury are almost invariably contaminated with micro-organisms. Proliferation of these micro-organisms can result in wound infection, which is associated with impaired healing (Edwards 2004).

Traumatic wounds range from simple abrasions and lacerations to open fractures, deep penetrating injuries and ballistic wounds. The severity of traumatic wounds and their risk of infection can depend on the traumatic mechanism that caused them. Higher energy wounds such as open fractures or wounds caused by munitions may be at high risk of wound infection, as they are typically more heavily contaminated than wounds caused by lower energy trauma and are associated with greater soft tissue damage. Soft tissue wounds account for approximately 5-10% of presentations to UK Emergency Departments (HSCIC 2014). Infection rates for traumatic wounds vary from around 15% in series of civilian open fractures (Dellinger 1988), to 30% in open tibial fractures resulting from combat trauma (Burns 2012). Infection in open fractures is associated with unplanned re-hospitalisation, delayed amputation and increased costs of medical care (Harris 2009).

Description of the intervention

Traumatic wounds judged to be sufficiently complex or contaminated often undergo surgery to excise contaminated or devitalised tissue, or both. Following this excision (or surgical debridement), most surgeons perform intraoperative fluid irrigation as part of an overall strategy to remove contaminating micro-organisms and to reduce the risk of subsequent wound infection.

Intraoperative fluid irrigation involves delivery of specific fluids into the wound. The type of fluids used to irrigate wounds fall into four broad categories:

1. chemically inert fluids, i.e. saline or water;
2. antiseptic solutions, e.g. chlorhexidine or iodine;
3. antibiotic solutions, e.g. bacitracin solution;
4. soap solutions, e.g. non-sterile castile soap.

These fluids can be delivered into the wound either by direct pouring, or via various devices including hand-held syringes or mechanised devices that generate pressurised streams of fluid. The pressure delivered by these devices varies. Theoretically, it needs to be sufficiently high to overcome the adhesive forces of contaminating bacteria and debris, but not so high as to cause further tissue damage (Nicks 2010). The effect of different fluid delivery systems is therefore also likely to influence irrigation efficacy, potential tissue damage and the volume of irrigation fluid used.

How the intervention might work

It is believed that the intraoperative application of fluids to a wound following surgical wound excision or debridement (i.e. removal of necrotic and foreign material; Brown 1978) exerts a physical effect which can remove micro-organisms from wound tissues. It is possible that the greatest effect occurs with the initial irrigation and that there is a diminishing effect with larger volumes of irrigation, but the optimum quantity of irrigation fluid is not known.

The possible mechanical action of fluid irrigation has been augmented by using solutions with active chemical properties (Petrisor 2008). Soap solutions, for example, are believed to disrupt the bonds between micro-organisms, thus assisting their removal from the wound bed (Anglen 2001). Conversely, some authors argue that the use of fluids other than saline or water can have a detrimental effect on tissues surrounding the wound, potentially slowing wound healing (Anglen 2005), or increasing the risk of wound infection (Fleming 1919). Similarly, it is hypothesised that high pressure fluid irrigation drives contamination deeper into tissues and causes further tissue damage, thereby promoting wound infection (Bhandari 1999).

Why it is important to do this review

There is current uncertainty about whether the use of intraoperative irrigation fluid is effective in preventing wound infection in traumatic wounds, whether one type of fluid is better than another, and what is the most effective delivery method (Petrisor 2008). A previous Cochrane review looked at water for cleansing both acute and chronic wounds (Fernandez 2012). It concluded that there is no evidence that the use of tap water to cleanse acute wounds impacts on the incidence of wound infection when compared to saline in adults and children. This review will examine the use of all irrigation fluid types for intra-operative removal of bacteria and contamination from traumatic wounds.

OBJECTIVES

To assess the effects of intraoperative fluid irrigation in preventing wound infection in traumatic wounds.

METHODS

Criteria for considering studies for this review

Types of studies

We will include all ongoing and completed single-centre or multicentre randomised controlled trials (RCTs). If we do not identify a single completed RCT, we will examine quasi-randomised studies.

Types of participants

We will include adults and children with traumatic wounds of the extremities or torso requiring inpatient management and surgical debridement in an operating theatre. We define a traumatic wounds as one resulting from injury, e.g. a gunshot wound, laceration, open fracture or bite. We will exclude burns, traumatic wounds with enteric contamination and those involving the central nervous system as we believe there are inherent differences between these wounds and other traumatic wounds that would lead to excessive heterogeneity. Specifically, enteric contamination has obvious implications with respect to the amount and type of bacteria in the wound compared to a wound located on an extremity, while the immunologically privileged nature of the central nervous system, that allows it to respond less aggressively to foreign material, is not analogous to the rest of the body. We will also exclude surgical wounds as they are not caused by trauma, and chronic wounds (e.g. ulcers) for the same reason. We will not separate adults and children as there is no evidence that there will be a substantially different immunological response to contamination in these groups.

We will exclude studies where participants are thought to already have an established wound infection at baseline.

Types of interventions

The interventions to be considered will be any type of intraoperative irrigation of a traumatic wound with a fluid. We will compare the following groups:

1. irrigation with fluid compared with no irrigation;
2. irrigation with one type of fluid/s compared with irrigation with another type of fluid/s;
3. irrigation with a lesser volume of fluid compared with irrigation with a greater volume of the same fluid.

Studies comparing the method of the delivery of the same fluid only will be excluded.

Types of outcome measures

We list primary and secondary outcomes below. If a study is otherwise eligible (i.e. correct study design, population and intervention/comparator) but does not report a listed outcome, then we will contact the study authors where possible to establish whether an outcome of interest here was measured but not reported.

Primary outcomes

Incidence of wound infection presented as number of participants with and without a recorded wound infection during study follow-up. There is no one standard definition of wound infection and we anticipate that studies might define presence of wound infection based on: clinical diagnosis, positive microbiological samples, requirement for surgical treatment and requirement for antibiotics. For the review we will accept the study authors definition of infection (recording details of this when recorded).

We will report outcome measures at the latest time point available for a study (assumed to be length of follow-up if not specified) and the time point specified in the methods as being of primary interest (if this is different from latest time point available).

Secondary outcomes

1. Time to primary or tertiary surgical wound closure.
2. Complete wound healing measured as time to wound healing or as a binary outcome of healed/not healed. We will accept study authors definitions of a healed wound.
3. Adverse events:
   i) direct surgical morbidity (death within 30 days, amputation, systemic infection, haematoma);
   ii) surgically-related systemic morbidity (chest infection, thromboembolic events (deep vein thrombosis and pulmonary embolism));
   iii) all cause mortality.
4. Mean length of hospital stay.

Search methods for identification of studies

Electronic searches

We will search the following electronic databases to identify reports of relevant randomised clinical trials:

1. The Cochrane Wounds Group Specialised Register;
2. The Cochrane Central Register of Controlled Trials (CENTRAL latest issue);
3. Ovid MEDLINE (1946 to present);
4. Ovid EMBASE (1974 to present);
5. EBSCO CINAHL (1982 to present).

The following search strategy will be used to search the CENTRAL database:

#1 MeSH descriptor: [Wounds, Penetrating] explode all trees
#2 MeSH descriptor: [Lacerations] explode all trees
#3 ((traumatic or puncture or penetrat* or crush* or gun shot or gunshot or knife or stab*) near/5 wound*):ti,ab,kw
#4 (avulsion or abrasion):ti,ab,kw
#5 {or #1-#4}
#6 MeSH descriptor: [Water] explode all trees
#7 MeSH descriptor: [Saline Solution, Hypertonic] explode all trees
#8 (water or saline or solution* or fluid* or irrigant*):ti,ab,kw
#9 MeSH descriptor: [Anti-Infective Agents, Local] explode all trees
#10 MeSH descriptor: [Chlorhexidine] explode all trees
#11 MeSH descriptor: [Iodine] explode all trees
#12 MeSH descriptor: [Povidone-Iodine] explode all trees
#13 MeSH descriptor: [Hypochlorous Acid] explode all trees
#14 MeSH descriptor: [Hydrogen Peroxide] explode all trees
#15 MeSH descriptor: [Benzalkonium Compounds] explode all trees
#16 MeSH descriptor: [Bacitracin] explode all trees
#17(antiseptic* or chlorhexidine* or iodine* or povidone* or hypochlorite or peroxide or ben?alkonium or bacitracin):ti,ab,kw
#18 MeSH descriptor: [Soaps] explode all trees
#19 MeSH descriptor: [Detergents] explode all trees
#20 (soap* or detergent*):ti,ab,kw
#21 MeSH descriptor: [Therapeutic Irrigation] explode all trees
#22 (wound near/5 (cleans* or decontaminat* or irrigat* or lavage or soak* or rins*)):ti,ab,kw
#23 {or #6-#22}
#24 #5 and #23

We will not apply restrictions relating to language, year of publication or type of publication.

We will combine the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision; Lefebvre 2011). We will combine the EMBASE search with the Ovid EMBASE filter developed by the UK Cochrane Centre (Lefebvre 2011). We will combine the CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2013).

Searching other resources

We will handsearch selected trauma, orthopaedic and plastic surgery conference proceedings (Appendix 1), along with the following registries of trials:

1. ClinicalTrials,gov (http://www.clinicaltrials.gov/);
2. World Health Organization (WHO) International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx);
3. European Union (EU) Clinical Trials Register Platform (ICTRP) (https://www.clinicaltrialsregister.eu/).

Additionally, we will search reference lists from literature reviews and identified clinical trials for citation of further studies.

Data collection and analysis

Selection of studies

Two review authors (JPB and RFR) will independently assess titles and abstracts to determine relevance and eligibility. We will exclude those studies that clearly do not meet the inclusion (eligibility) criteria and obtain full text copies of potentially relevant references. Two review authors (JPB and RFR) will independently assess the eligibility of retrieved papers. We will resolve disagreements by discussion between review authors or by appeal to a third reviewer (MM). Where the eligibility of a study is unclear we will attempt to contact study authors. We will document reasons for exclusion. We plan to translate any non-English articles before assessment, as needed. We will complete a PRISMA flowchart to summarise this process.

Where studies have been reported in multiple publications/reports, all associated publications will be obtained. Whilst the study will be included only once in the review, data will be extracted from all reports to ensure all available relevant data are obtained.

Data extraction and management

Two review authors (AP and YFC) will independently extract data from each study using a data extraction form modified from the Cochrane Wounds Group data collection form. We will cross-check extracted data and resolve discrepancies by consensus. Where consensus cannot be reached, a third review author (JB) will be consulted . The extraction of data will include study design, demographics, settings, types and features of the traumatic wounds, details of the intervention (irrigation fluids used and methods of delivery) and comparator, methods of wound closure, concomitant treatment, length of follow-up, number of participants withdrawn or lost to follow-up and reasons for withdrawal, methods of outcome assessment and findings.

Assessment of risk of bias in included studies

Two review authors (JPB and RFR) will independently assess the risk of bias of included studies. We will resolve disagreements by discussion between these two authors or by appeal to a third review author (YFC). We will assess the risk of bias in RCTs using the Cochrane risk of bias tool, examining the seven domains of sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and 'other' potential sources of bias. We will categorise bias as low risk, unclear risk or high risk using the definitions provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Measures of treatment effect

Risk ratios (RR) will be calculated for dichotomous outcomes (such as incidence of infection) with two exceptions. Firstly, when the event rate is found to be very low (less than 1%), we will adopt Peto one-step odds ratio method as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Section 16.9.5; Higgins 2011).

Hazard ratios (HR) will be calculated for time-to-event data (such as time to wound closure). We will present continuous data (such as length of hospital stay) as mean differences (MD). All data will be presented with 95% confidence intervals (CI).

Unit of analysis issues

We expect that the unit of randomisation and analysis will be individual participants in the majority of eligible studies. We will record any incidence where a study included participants with multiple wounds and used individual wounds rather than the individual participant as the unit of analysis. If cluster trials are found, we will firstly seek data that properly account for the cluster design and include them in meta-analysis using the generic inverse-variance method. If this is not possible, we will attempt to correct unit of analysis errors by using the approximate analysis method described in the *Cochrane Handbook for Systematic Reviews of Interventions* (section 16.3.4; Higgins 2011).

Dealing with missing data

It is common to have data missing from trial reports. Excluding participants from the analysis post randomisation or ignoring participants who are lost to follow-up compromises the randomisation and potentially introduces bias into the trial. If it is thought that study authors might be able to provide some missing data, we will contact them; however, it is likely that data will often be missing because of loss to follow-up. In individual studies, when data on the incidence of wound infection or healing are presented, we plan to assume that randomly assigned participants not included in an analysis had a non-infected or a healed wound at the end of the follow-up period (i.e. they will be considered in the denominator but not in the numerator).

When a trial does not specify participant group numbers before dropout, we will present only complete case data.

For continuous variables e.g. length of hospital stay and for all secondary outcomes we will present available data from the study reports/study authors and do not plan to impute missing data. Where measures of variance are missing we will calculate these wherever possible. If calculation is not possible we will contact

study authors. Where these measures of variation remain unavailable and cannot be calculated the study will be excluded from any relevant meta-analyses that are conducted.

Assessment of heterogeneity

Assessment of heterogeneity can be a complex, multi-faceted process. Firstly, we will consider clinical and methodological heterogeneity: that is the degree to which the included studies vary in terms of participant, intervention, outcome and characteristics such as length of follow-up. This assessment of clinical and methodological heterogeneity will be supplemented by information regarding statistical heterogeneity - assessed using the Chi² test (a significance level of $P < 0.10$ will be considered to indicate statistically significant heterogeneity) in conjunction with I^2 measure (Deeks 2011). I^2 examines the percentage of total variation across RCTs that is due to heterogeneity rather than chance (Higgins 2003). Very broadly we will consider that I^2 values of 25%, or less, may mean a low level of heterogeneity (Higgins 2003), and values of more than 75%, or more, indicate very high heterogeneity (Deeks 2011). We will also examine the variability of the point estimates and the overlap of the confidence intervals, when I^2 values are less than 50%. Where there is evidence of high heterogeneity we will attempt to explore this further: *see* Data synthesis.

Assessment of reporting biases

We will inspect funnel plots in order to detect potential publication and reporting biases or other small study effects. We will test funnel plot asymmetry using a recommended method (Peters 2006), if ten or more studies are included in the analysis.

Data synthesis

Details of included studies will be combined in a narrative review according to the comparison between intervention and comparator, the population and the time point of the outcome measurement. Clinical and methodological heterogeneity will be considered and pooling undertaken when studies appear similar in terms of wound characteristics, intervention type, method of delivery and outcome assessment.

In terms of meta-analytical approach, in the presence of clinical heterogeneity (review author judgement) and/or evidence of statistical heterogeneity we will use the random-effects model. We will only use a fixed-effect approach when clinical heterogeneity is thought to be minimal AND statistical heterogeneity is estimated as statistically not significant for the Chi-Squared value and 0% for the I^2 assessment (Kontopantelis 2012). This approach will be adopted as it is recognised that statistical assessments can miss potentially important between-study heterogeneity in small samples, hence the preference for the more conservative random effects model (Kontopantelis 2013). Where clinical heterogeneity is thought to be acceptable or of interest we may meta-analyse even when statistical heterogeneity is high but we will attempt to interpret the causes behind this heterogeneity and will consider using meta-regression for that purpose, if possible (Thompson 1999; Thompson 2002)

Data will be presented using forest plots where possible. For dichotomous outcomes we will present the summary estimate as a risk ratio (RR) with 95% CI. Where continuous outcomes are measured in the same way across studies, we plan to present a pooled mean difference (MD) with 95% CI; we plan to pool standardised mean difference (SMD) estimates where studies measure the same outcome using different methods. For time to event data, we plan to plot (and, if appropriate, pool) estimates of hazard ratios and 95% CIs as presented in the study reports using the generic inverse variance method in RevMan 5.3 (RevMan). Where time to healing is analysed as a continuous measure but it is not clear if all wounds healed, use of the outcome in the study will be documented but data will not be summarised or used in any meta-analysis.

Summary of findings tables

We will present the main results of the review in 'Summary of findings' tables. These tables present key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined and the sum of available data for the main outcomes (Schunemann 2011a). The 'Summary of findings' tables also include an overall grading of the evidence related to each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach. The GRADE approach defines the quality of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The quality of a body of evidence involves consideration of within trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Schunemann 2011b). We plan to present the following outcomes in the 'Summary of findings' tables for each comparison:

- wound infection;
- wound healing.

Subgroup analysis and investigation of heterogeneity

If sufficient data are available, we will carry out the following prespecified subgroup analyses:

1. open fractures versus wounds without underlying fractures;
2. limb wounds versus torso wounds;
3. ballistic wounds versus other types of wounds

Sensitivity analysis

Pending sufficient data, we will carry out sensitivity analyses by:

1. excluding studies with high or unclear risk of selection bias (methods of randomisation, allocation concealment);
2. excluding studies with high or unclear risk of detection bias (blinding of outcome assessment).

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. List of handsearched conference proceedings

We will search abstracts from all available conference proceedings from the following societies:

1. Orthopaedic Trauma Association (OTA)
2. British Orthopaedic Association (BOA)
3. British Association of Plastic and Reconstructive Surgeons (BAPRAS), formally British Association of Plastic Surgeons (BAPS)
4. American Academy of Orthopaedic Surgeons AAOS Annual meeting
5. British Trauma Society (BTS) Annual Meeting
6. European Society for Trauma and Emergency Surgery (ESTES), previously ESTAS and ETS
7. American Association for the Surgery of Trauma (AAST)
8. Eastern Association for Surgery of Trauma (EAST)
9. Western Association for Surgery of Trauma (WEST)
10. International Confederation for Plastic, Reconstructive and Aesthetic surgery (IPRAS)
11. American Association of Plastic Surgeons (AAPS)

CONTRIBUTIONS OF AUTHORS

Jowan Penn-Barwell: conceived the review question and developed and coordinated the protocol. Wrote and edited the protocol. Advised on the protocol. Approved the final version of the protocol and is the guarantor of the protocol.

Aikaterini Peleki: conceived the review question and developed the protocol. Performed part of writing and editing the protocol. Approved the final version of the protocol prior to submission.

Yen-Fu Chen: developed the protocol. Performed part of writing and editing the protocol. Approved the final version of the protocol prior to submission.

Jonathan Bishop: completed the first draft of the protocol, advised on the protocol, and approved the final version prior to submission.

Mark Midwinter: conceived the review question. Edited the protocol, made an intellectual contribution and advised on the protocol. Approved the final version prior to submission.

Rory Rickard: conceived the review question and developed the protocol. Completed the first draft of and edited the protocol, made an intellectual contribution and advised on the protocol. Approved the final version prior to submission.

Contributions of editorial base:

Jo Dumville: advised on methodology, interpretation and protocol content. Approved the final protocol prior to submission.
Sally Bell-Syer: coordinated the editorial process. Advised on methodology, interpretation and content. Edited the protocol.

DECLARATIONS OF INTEREST

JPB: nothing to declare

AP: nothing to declare

YFC: nothing to declare

JB: nothing to declare

MM: nothing to declare

RFR: nothing to declare

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NOTES